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THE GENETICS OF ARTHROGRYPOSIS IN CHAROLAIS CATTLE

BY

© LAKSIRI ANURA GOONEWARDENE

A THESIS
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THE UNIVERSITY OF ALBERTA

FACULTY OF GRADUATE STUDIES AND RESEARCH

The undersigned certify that they have read, and recommend to the Faculty of Graduate Studies and Research, for acceptance, a thesis entitled, "The Genetics of Arthrogryposis in Charolais Cattle" submitted by Laksiri Anura Goonewardene in partial fulfilment of the requirements for the degree of Master of Science.

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ABSTRACT

Arthrogryposis is an inherited abnormality which causes crippling of the limbs in new born calves and is sometimes associated with a cleft palate. The mode of inheritance of the defect is due to an autosomal recessive gene showing incomplete penetrance. Research from Charolais herds in France indicate the gene to be at a high and stationary frequency. The thesis deals with the genetics of the abnormality and views it from an evolutionary stand point. At the University of Alberta Beef Breeding Station, 20 proven carrier dams and 26 crippled calves have been observed. Two genetic studies are reported one of which involves the 20 carrier dams and the other involving both suspected and proven carrier males and females. The studies indicate a recessive form of inheritance and a high degree of penetrance of the recessive gene in the populations studied. Results from this herd and others in the neighbourhood indicate the recessive gene to be distributed in populations by two types of carriers namely the heterozygous and homozygous recessive carriers. Four probable homozygous recessive sires have been identified which themselves show near zero penetrance of the gene. All four have been pure Charolais bulls while all defective progeny have been Charolais crossbreds. The penetrance of the defective gene among Charolais crossbreds seems to be near complete and the expressivity of the defect variable. A series of selective modifier genes may be responsible for the supression of the defect in pure Charolais herds which could be the

reason why homozygous sires survive. However, when the resulting progeny are crossbred the defect is expressed more completely due to the absence of these modifier genes.

The fertility and longevity of the 20 proven carrier dams were compared with a control population of the same origin and genetic background over an 11 year period. Fertility was estimated by the number of missed calving opportunities a dam had throughout her breeding life and longevity estimated by the number of dams culled in the two populations during the experimental period. Both fertility and longevity were superior in the carrier herd compared to the control, ($P < 0,01$). The Charolais breed has evolved two mechanisms by which they can overcome the inherent survival problem that some calves have and help keep the recessive gene at a relatively high frequency, by carrier dams showing a selective advantage due to the better reproductive fitness they possess and by complete suppression of the defect among homozygous recessive sires due to the selection of favourable modifier genes. Some practical applications of arthrogryposis and methods by which one could utilize some of its good effects are also discussed in the thesis.

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1. GENERAL INTRODUCTION

Many inherited abnormalities which have economic importance have been observed in cattle. These abnormalities may cause malformations or death during early or late embryonic development, at birth or their expression may be delayed and detected subsequently in the adult animal.

Abnormalities at birth may be either genetic or environmental. An environmental basis is indicated almost always when, the defect occurs in relation to a particular environment and when it could be corrected by providing the required conditions. Also, if the defect occurs following a period of stress and corrects itself naturally when the stress period is over, an environmental basis is implicated. On the other hand a genetic basis is indicated when, (a) the defect occurs independent of environment, (b) is confined to one breeding group or family, (c) when inbreeding tends to increase the chances of the defect being brought out, or (d) when research on similar conditions with large numbers of animals have indicated a genetic basis.

Genetic abnormalities arise most often due to mutations which could take various forms, such as point or gene mutations, chromosomal aberrations, translocations or inversions. These abnormal conditions may be inherited as autosomal or sex linked dominants or recessives involving one or more gene loci.

Arthrogryposis affecting Charolais cattle is reported to be inherited as an autosomal recessive and is often associated

with a cleft palate. The disease is becoming more important in recent times as the frequency of the recessive gene appears to be high in Charolais populations. Furthermore, when the defect results in lethality, especially in the calves having a cleft palate, it is of much economic importance.

The objectives of this study were to investigate further the genetics of the defect, and to find out why such a gene persists in populations at a high frequency in spite of its adverse effects. The possible control or utilization of the gene will also be explored.

The reliability of such a study would depend on the number of animals available. Data where carriers are identified, matings are planned, breeding records and pedigree analysis of deformed calves are possible paying due attention to environmental factors if any, can be useful in establishing the mode of inheritance and can provide a better understanding of the genetics of arthrogryposis.

2. REVIEWS OF LITERATURE

2.1 Arthrogryposis and related defects in various breeds of cattle

Arthrogryposis, crippling or restricted limb movement in cattle have been reported in breeds such as the Jerseys (Spielman, et al.,1944), Guernsey (Freeman, 1958), Australian Illawara, Ayrshire, Friesian crosses (Whittem, 1957), Friesians (Hutt, 1934), and many other breeds. The external manifestations of the defect differs very much and in some instances both pairs of limbs are affected while at other times only one pair of limbs is affected. Sometimes, both muscle and skeletal elements are involved.

Hutt (1934) recognized a lethal condition in Friesian cattle which caused extreme rigidity in the limbs and neck due to the contracture of the muscles in these areas. The condition was put down as being inherited as a simple autosomal recessive, where the defect is spread through carrier sires and dams. A non-genetic form of a similar defect in Friesian cattle was also reported and described by Mead, et al. (1934). Among Friesian cattle in New Zealand, crippling associated with ankylosis[1] and hydropic amnion is reported by Murray (1951).

Blood (1956) reported the details of thirty five cases of arthrogryposis in new born calves. He reported the clinical findings in 35 cases of arthrogryposis and 5 cases of hydranencephaly[2] associated with blindness in the new born calves. Blood

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1. Abnormal immobility and consolidation of a joint caused due to faulty bone structure or by the destruction of membranes that line the joint.
2. Absence of cerebral hemispheres, their normal site being occupied by fluids.

(1956) maintained that the two conditions are different manifestations of the same disease. The arthrogrypotic calves showed restrictions in movements mainly in the joints of the limbs and of the neck, while the bones remained unaffected. The defective calves had a lower bulk of muscle in the affected areas, the muscle masses were paler in colour and altered in consistency. Those calves showing hydranencephaly indicated various degrees of brain abnormality and in some instances the cerebral hemispheres were reduced to fluid filled sacs. The author puts down these histological findings as a state of neurogenic muscular atrophy in the affected calves. Blood (1956) attributed the cause to be environmental and a genetic basis is ruled out.

Whittem (1957) described 29 cases of arthrogryposis in the county of Cumberland, N.S.W., Australia. Of the 29 cases 23 showed arthrogryposis and 15 calves showed blindness. No attempt was made in this study to ascertain breed differences and the 29 cases reported consisted of Illawara Shorthorns, Ayrshires, Friesians and Friesian crosses. The clinical findings were similar to those reported by Blood (1956). Whittem (1957) indicated an environmental basis for this group of abnormalities and attributed it to causal agents such as infections toxins and nutritional factors.

Shupe, James, Balls, Binns and Keeler (1967) reported investigations of a skeletal congenital malformation, believed to be hereditary in origin in Hereford cattle. The abnormal

calves showed various degrees of arthrogryposis, kyphosis[3], torticollis[4], scoliosis[5] and a cleft palate. The incidence of the defect was one out of four in certain mating combinations. Shupe, et al. (1967) suggest that the deformity was due to a simple autosomal recessive gene.

Freeman (1958) reported a case of curved limbs in Guernsey cattle from the Iowa state college herds. The deformity involved both muscle and skeletal growth and the rear limbs showed gross deformity. Freeman (1958) suggests the defect to be inherited as a simple autosomal recessive but that the data were inadequate to exclude a more complicated hypothesis. Longer gestation periods are reported in the carrier dams.

A type of hereditary congenital flexed pasterns was reported in an inbred herd of Jersey cattle, Mead, Gregory and Regan (1943). The defect is characterized by deformities in the fore and sometimes in the hind limbs, but never in the hind limbs alone. The abnormality is expressed in various degrees and in some instances as the calf gets older the flexion becomes less and less until the limbs become normal. Mead, et al. (1943) suggest a genetic and a non genetic mode of inheritance for the same defect, both types having similar phenotypic manifestations. The genetic form is inferred to be due to an autosomal recessive gene by the same authors.

Spielman, Hill and McGullock (1944) report on 69 cases of muscular contracture among Jersey herds in California. They

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3. Abnormally increased convexity in the curvature of the thoracic spine - "hunchback".

4. A contracted state of the cervical muscles producing tortion of the neck - "wryneck".

5. Lateral curvature of the vertebral column.

stated that although considerable variation occurs in the appearance of these abnormalities both lethal and sub lethal, the gross manifestations seem to be various degrees of muscular contracture and ankylosis, and in most cases the fore limbs seemed to be the first to be affected. Fairly close inbreeding also brought out the defect more frequently. Spielman and Hill and McGullock (1944) withhold their final judgement on the mode of inheritance as some of the dams had an unfavourable pre-natal environment.

A deficiency of manganese was reported to have caused an arthrogrypotic condition and a bent spine 'torticollis' among calves in the United States, Dyer and Rogas (1965). Manganese is known to be involved in cartilage and bone formation, growth and function of the nervous tissue, Dyer and Rogas (1965). A relationship between low levels of manganese and the incidence of the disease in gestating cows is also reported by the same authors suggesting the defect to be due to an environmental cause. A form of arthrogryposis with histologic changes involving the nervous and muscular tissue have been reported in many breeds of cattle, by many workers (Blood, 1956; Whittem, 1957; Herzog and Adam, 1968; Nes, 1953). However, a similar condition without these associated defects has also been reported. Arthrogryposis associated with torticollis, scoliosis and kyphosis was reported in Hereford cattle by Shupe, et al. (1967), and in other breeds by Dyer and Rogas (1965), King (1965) and Mead, et al. (1943). Arthrogryposis and its association with other conditions

has also been reported: ankylosis and hydropic amnion[7] (Murray, 1959), hydranencephaly among Ayrshires, Shorthorns, Friesians and Friesian crosses (Whittem, 1957). The general defect occurs in association with spinal bifida[6] and segmental aplasia as reported by Nes (1953), Whittem (1957), and Blood (1956). The absence of the ventral horn cells of the spinal cord on histologic examination was also shown by both Blood (1956), and Whittem (1957). Furthermore, crippling of the limbs associated with a cleft palate is reported in Jersey cattle (Spielman and Hill, 1944), in Herefords (Shupe, et al., 1967), and among Charolais cattle (Lauvergne and Blin, 1967; Liepold, et al., 1969).

In scientific literature arthrogryposis and similar conditions have been referred to by many names such as neuromyodysplasia congenita (Herzog and Adam, 1968), amyoplasia myodystropia foetalis, and the common name 'the crooked calf disease' (Blood, 1956).

In general therefore, arthrogryposis occurs in many breeds of cattle the cause in some instances being genetic, while at other times it is environmental. The defect occurs associated with other conditions which could be detected as gross abnormalities such as a cleft palate, or others which involve changes in skeletal, muscular and nervous tissue which can be detected by a histological examination. The external manifestations of the defect however seem to vary from breed to breed.

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6. A defect of the vertebral column due to the imperfect union of the paired vertebral arches at the mid line.
7. Amnion affected with dropsy.

2.2 Arthrogryposis in Charolais cattle

2.2.1 Description of the abnormality

A form of arthrogryposis affecting the limbs of Charolais calves has been reported (Lauvergne and Blin, 1967; Liepold, et al., 1969; Singh and Little, 1971). The defect is often associated with a cleft palate which is prominently large (Lauvergne and Blin, 1967; Liepold, et al., 1969). The affected calves are born dead or alive and there is no apparent relationship between the severity of the defect and whether or not the calves are born dead or alive (Liepold, et al., 1969).

Liepold, et al. (1969, 1970) subjected affected calves to clinical as well as a necroscopic examination to observe and report on the gross abnormalities as well as the histologic changes that could be detected microscopically, the latter examination being done on the muscles, nervous system including the brain and spinal cord, the bones and joints, endocrine glands and the myocardium. Twelve crippled calves were studied of which ten were females and two were males. The authors reported that the pedigrees of the twelve calves indicated 50% or more Charolais breeding. The gross abnormalities included various degrees of the defect, eight out of the twelve showing the involvement of all four limbs together with a cleft palate. Of the animals examined one calf had all four limbs affected without a cleft palate while three showed involvement of the fore limbs only, without a cleft palate (Liepold, et al., 1969). In the calves affected, the fore limbs showed flexion at the carpel

and fetlock joints while the hind limbs showed either flexion or over-extension at the hock and fetlock joints. The degree of flexion and/or over extension of the limbs varied between the calves examined and some calves showed normal hind limbs void of abnormalities but passive extension of the hock joint was not possible. The fetlock joints of the hind limb showed more mobility than the other joints in the fore and hind limbs and in almost every case where the hind limbs were affected, they could be flexed and extended without too much difficulty. The same authors reported that some arthrogrypotic calves showed a considerably smaller knee cap and an abnormally shaped cannon bone. All in all, the affected calves showed more prominent limb joints due to the marked reduction in the muscles. The deformed calves, especially those with a cleft palate if unassisted do not survive for more than a few days and a majority of them die due to secondary respiratory conditions such as pneumonia. The defective calves show a normal eye and withdrawal reflex while the patellar reflex, extensor thrust and cutaneous trunci reflexes were usually absent. However, sensory perception was reported as being present in a majority of defective calves.

2.2.2 Abnormalities in muscles

Liepold, et al. (1969, 1970) reported that muscle masses in the affected areas were reduced in size and lacking in tone. In the fore limb the supraspinatus, infraspinatus, and the biceps brachii were reduced and paler in colour while in the hind limb

the gastrocnemius was often affected. The authors state that the degree of severity varied between muscles some being more affected than others. Gross lesions showed haemorragic spots throughout the affected muscles, a paler colour and such muscles floated in water.

On microscopic examination the same authors report that the muscle fibres in each bundle were reduced in diameter throughout the sarcolemma while the nuclei and cross striations were normal. Liepold, et al. (1970) also report that the spaces in the muscle bundles were replaced by adipose tissue and that muscle regeneration was absent in the areas examined. Furthermore, when the defective muscle masses were severed limb movement was possible.

2.2.3 Lesions in the nervous tissue

Liepold, et al. (1969, 1970) report that tissues of the nervous system showed abnormal lesions along with those of the muscles and the lungs. The authors reported that the most striking defect occurred in the cervical region of the spinal cord. The central canal was dilated to several times its normal diameter and posterior to the dilated segments the central canal showed extreme narrowness. A second form of abnormality referred to as syringomyelia was found, in the region of the cord, where cavitations occurred in the grey matter adjacent to the central canal. Blunt short ventral grey horns were observed during the examination in the affected cervical segments and the grey matter extended in the segments

where the central canal was dilated, while the grey matter was reduced and extremely thin, around the segments where the central canal was reduced. In general, lesions in the spinal cord, degenerative changes in the nervous tissue, gliosis[8] and neuronal atrophy was observed in the deformed calves.

2.2.4 Inheritance of arthrogryposis

The probable mode of inheritance of arthrogryposis in Charolais cattle has been investigated by Lauvergne and Blin (1967), (1968), and by Liepold, et al. (1969) (1970).

Lauvergne and Blin (1967) attributed the defect to the action of a dominant gene showing incomplete penetrance. Lauvergne and Blin (1968) attribute the cause of arthrogryposis associated with a cleft palate to an autosomal recessive gene showing incomplete penetrance. They said the gene was common in Charolais populations and abnormal subjects may be born even when cross breeding is practiced. Another reason to favour a recessive mode of inheritance was that two recognized carrier bulls at the Artificial Insemination Centre, Allier, France did not produce a single defective calf when bred to 23,000 non Charolais females, Lauvergne and Blin (1968).

Liepold, et al. (1970) attributed the defect to a recessive gene having evolved due to a mutation in Charolais cattle. They report the arthrogryposis gene to be fairly stationary at a low frequency in Charolais cattle in Canada. Lauvergne (1972-73) estimates a gene frequency of 0.2 to be fairly stationary in French Charolais herds. He estimated the penetrance of the

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8. Increase in the number of glial cells.

gene in homozygotes to range from 0.14 among males to 0.1 among females. He reported that the transmitters of the defect cannot be distinguished from the exterior and that these carriers especially the dams appear to show some form of hybrid vigour in characters associated with reproduction. Eradication of the gene from Charolais herds was not recpmmended, Lauvergne (1972-73) but with an adequate female population having a high enough genetic frequency it was considered possible to discover clean bulls which did not carry the defective gene.

2.2.5 Conclusion

In conclusion the literature on arthrogryposis in Charolais cattle indicate the defect to be caused by the action of an autosomal recessive gene showing incomplete penetrance, which appears to be at a high and stationary frequency in Charolais populations. The defect is expressed in various degrees of severity with one or both pairs of limbs being affected and sometimes associated with an incompletely developed palate. The condition is also characterized by lesions of the muscular and nervous tissue. The defect appears to be a nerve induced form of muscular atrophy.

3. EXPERIMENTAL STUDY OF ARTHROGRYPOSIS IN CHAROLAIS CATTLE

3.1 Source of data

The data used in this thesis come from the Beef Cattle Research Ranch at Kinsella, Alberta maintained by the University of Alberta. To date, in this herd, 26 calves showing arthrogryposis have been born to 20 dams, between 1966 and 1973.

3.2 Experimental herd history

A population referred to as the 'cripple herd' consisting of both proven and suspected carriers is being maintained on the Research Ranch. The cripple population originated from a hybrid line which was established in 1961, by combining three main breeds namely, Angus, Charolais and Galloway, (Berg, 1973). After initial mixing of the three foundation breeds and by A.I. sampling with Charolais bulls, the population has evolved to contain a proportion of 33% Angus, 36% Charolais and 23% Galloway in 1972. Table 1 gives the breed percentages in the hybrid line from 1962 to 1972 at four year intervals. The breeding practice in the hybrid line has been to maintain it as a closed herd during the last number of years.

The cripple population was derived from the hybrid line; as soon as a dam gave birth to a crippled calf she was removed from the hybrid line and maintained in the cripple population. During the latter years a number of suspects, usually sons and daughters of carrier sires or dams were added to the cripple herd. The cripple herd is maintained as a separate line and the

Table 1: Average breed percentages of hybrid calves born at Kinsella from 1962-1972
Source (Berg, 1973)

Breed	1962	1966	1970	1972
Angus	41.4	41.6	37.6	33.0
Charolais	16.8	29.8	35.1	36.3
Galloway	40.3	26.4	20.3	23.2
Brown Swiss	-	0.6	4.7	3.3
Others	1.5	1.6	2.3	4.2

breeding practice is to mate suspected and known carriers in a series of planned matings in order to establish the mode of inheritance of arthrogryposis. Thus the individuals in the cripple herd that were derived from the hybrid line would be different in that they either have given birth to a defective calf or are strong suspects of being carriers of arthrogryposis but, the two lines the cripple and the hybrid have the same origin and genetic background.

3.3 General management

On the ranch all dams are usually exposed to breeding on pasture during the summer (July and August) so that they calve during spring (April and May) the following year. The dams are wintered in groups, the mature cows separate from the one and two year olds. During winter heifers and cows are fed a minimum maintainance ration of grain, straw and hay. Cows normally lose 20 to 60 lbs. on an average from December to March, while heifers are wintered to gain 20 to 40 pounds. Winter feeding begins in December and goes through to March. Calving begins in April and supplementary feeding is done during calving if and when necessary. Two year old heifers are calved in a feed lot to control any calving problems while the mature cows are calved in the open range. After calving the heifers are put on pasture and grain supplementation continued at the winter rate for flushing until the next breeding season, (Berg, 1973).

3.4 Introduction of the defective gene into the Kinsella herds

By examining the pedigrees of the crippled calves and their immediate ancestors, it became very evident that the gene was introduced by way of pure Charolais bulls that have been used extensively in the hybrid line during the early years. Six such bulls have been recognized which have passed on the defective gene to their offspring resulting in crippled calves, in some instances after several generations. The bulls A, B and C are the older Charolais bulls which have introduced the arthrogryposis gene while 67146, 67179 and 69115 are three recognized carriers identified from within the herd.

Key to pedigrees:

The following key should be observed when looking at the pedigrees.

(1) The number or letter denoting the name of the sire appears first, at the top left hand corner.

(2) All proven carrier males and strong suspects are underlined.

(3) A (*) indicates that this dam when mated to the above sire gave birth to a crippled calf.

(4) ------- indicates the probable carrier sire being far back in the pedigree.

(5) Alphabetic letters in ( ) denotes breed or approximate breeding of sire or dam,

GA---Galloway HE---Hereford

AN---Angus

CH---Charolais

In these breeding records an attempt is made to identify the way in which the defective gene was introduced into the herd. Hence, pedigrees may be incomplete and the pedigrees of the carrier sires themselves are not shown. The immediate ancestors of 21 crippled calves are shown.

3.4.1 Sire A and his crippled progeny

Referring to Chart A, sire A has been responsible for the birth of four crippled calves three of which were obtained when it was bred to his own daughters. Thus these three dams 66107, 66135 and 66224 in all probability received the defective gene from sire A. If sire A was heterozygous, there is only a 50% chance of its daughters being carriers and if he was homozygous recessive all its offspring would be carriers. Dam 61907 in all probability received the defective gene from sire B which was her sire. This set of pedigrees indicate the defective gene to be brought in through one purebred Charolais sire and the other carrying 87.5% Charolais breeding.

3.4.2 Sire 67146 and his crippled progeny

Sire 67146 has been responsible for two crippled births and the pedigrees (Chart B) indicate the introduction of the defective gene to be through sire B and/or sire C which have been the grand sires of dam 64122 and the sire of dam 61912. This pedigree also indicates the probable introduction of the recessive gene to be through sire B and sire C.

Chart A

Pedigrees of Sire A and his crippled progeny

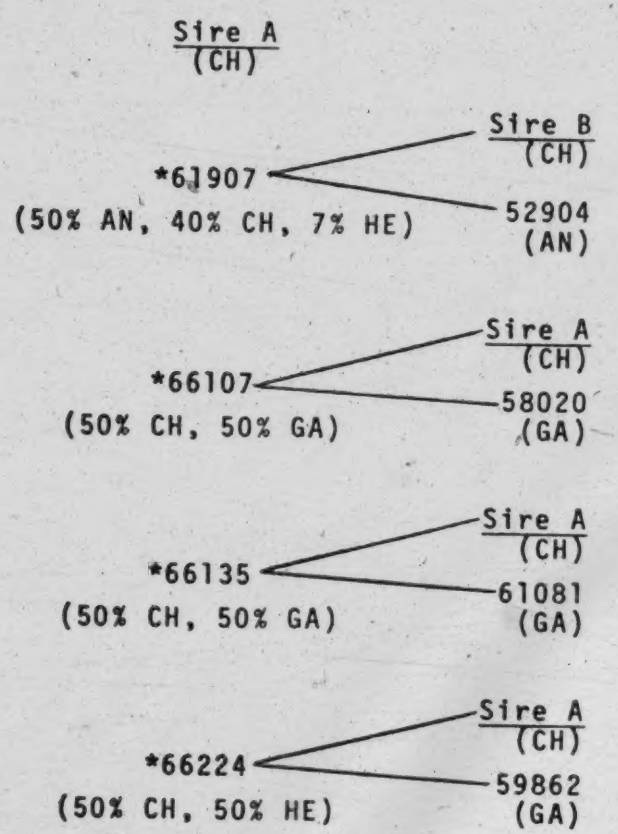
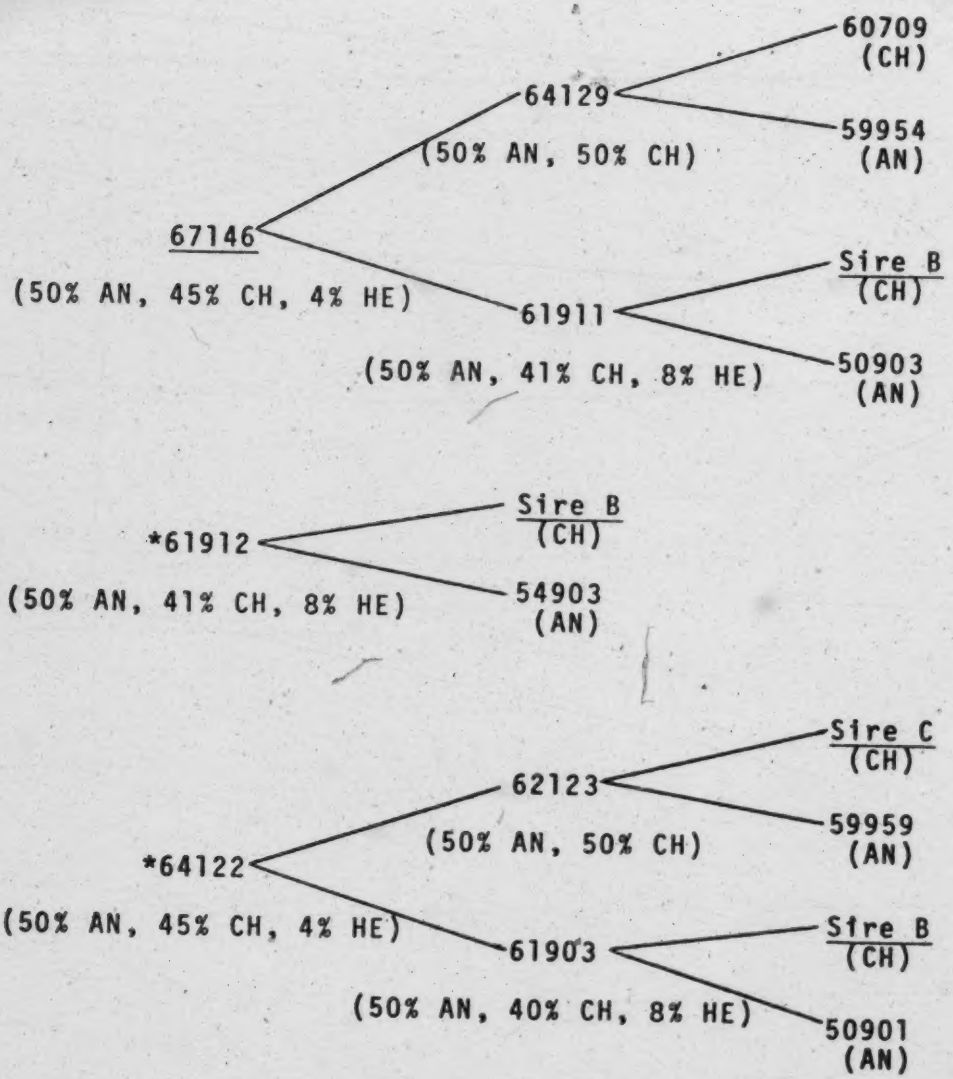


Chart B

Pedigrees of Sire 67146 and his crippled progeny



3.4.3 Sire 67179 and his crippled progeny

This sire has been used quite extensively for breeding in the cripple herd and has been responsible for 7 crippled calves. Referring to dams 61911, 61912, 62101 and the sire himself, the recessive gene was most probably introduced through sire B and/or sire C which appear in various positions in the pedigrees. Dam 66135 would have in all probability received the gene from sire A who was her sire and is a confirmed carrier of the recessive gene. However, with the other three dams the case does not seem to be so clear as the sires that have directly been involved in the introduction of the defective gene have not been in their pedigrees. It seems probable that the gene was introduced by sire 64134 which is common to all three dams. Sire 64134 had as one of its ancestors sire B which has been recognized as a carrier of the recessive gene.

3.4.4 Sire 69115 and his crippled progeny

This sire has been responsible for 8 crippled calves and has been identified as a carrier. Looking at the pedigrees of the dams, both sires B and C have been used for breeding in the earlier generations and the defective gene may have been introduced through these two sires as well as another proven carrier sire 67146 which occurs in some of the pedigrees.

If the mode of inheritance of arthrogryposis is of an autosomal recessive type, if a crippled calf is obtained both parents must be carriers. Hence, the recessive gene would be introduced separately from the sires side as well as from the dams side. In other words, both parents would contribute equally in order

Chart C

Pedigrees of Sire 67179 and his crippled progeny

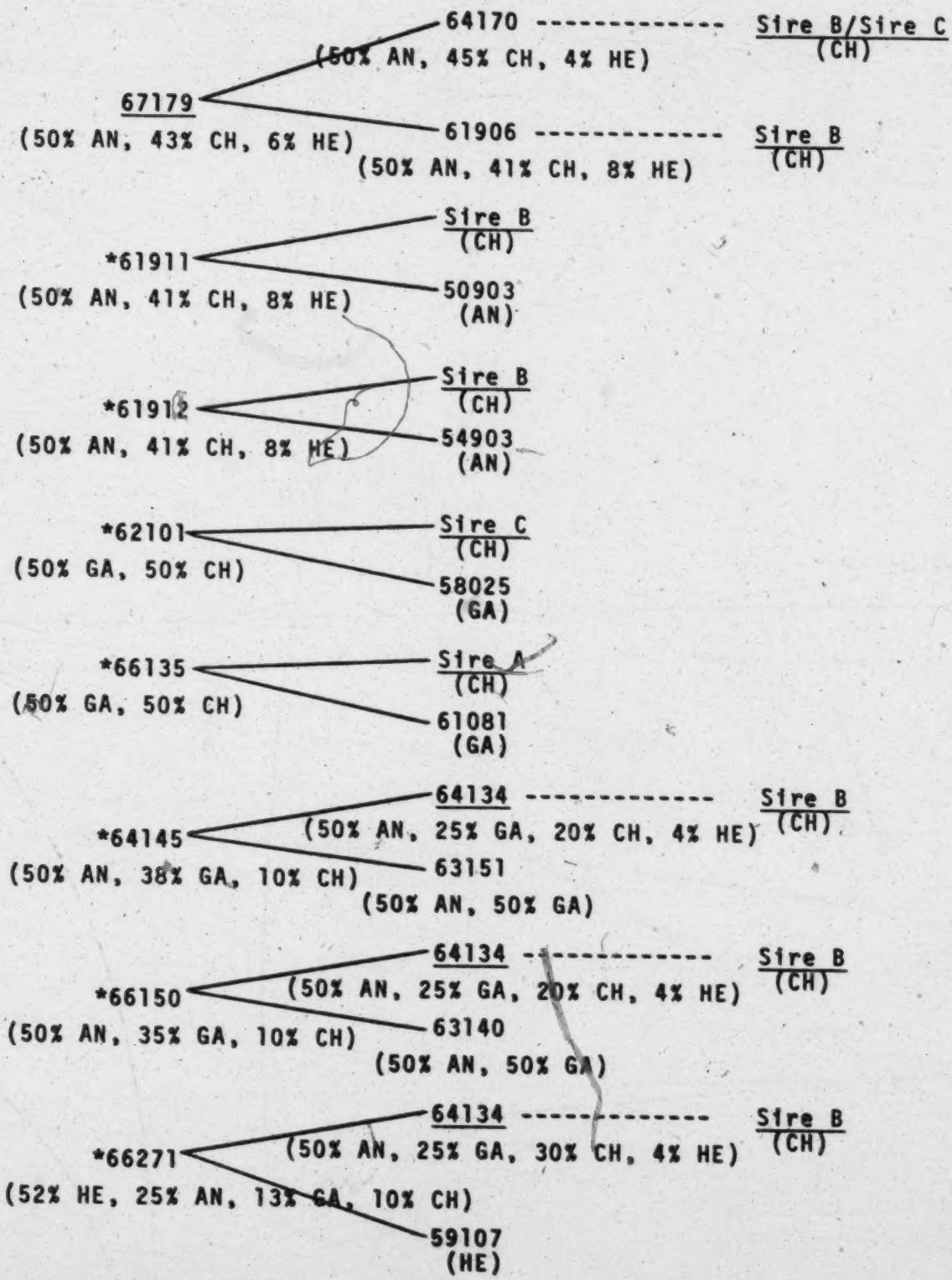


Chart D

Pedigrees of Sire 69115 and his crippled progeny

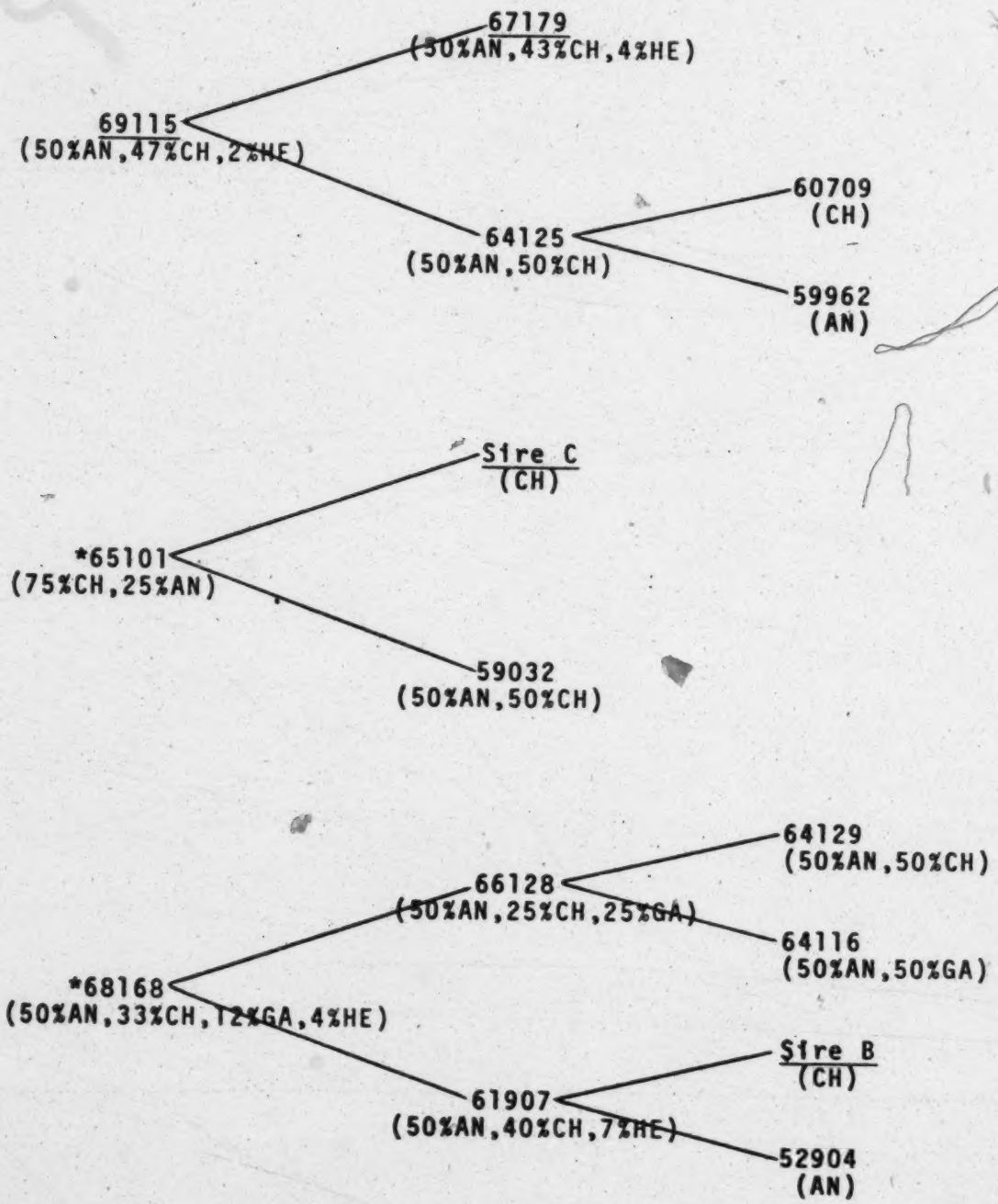
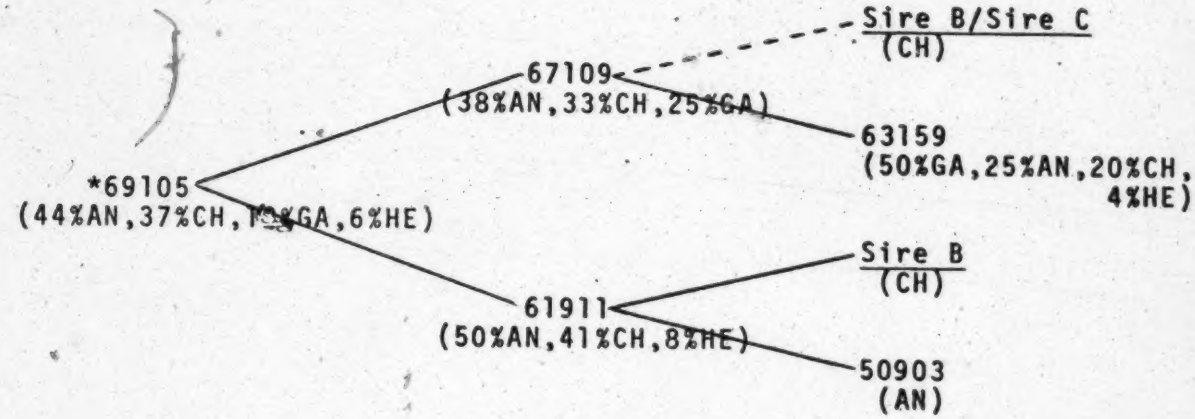
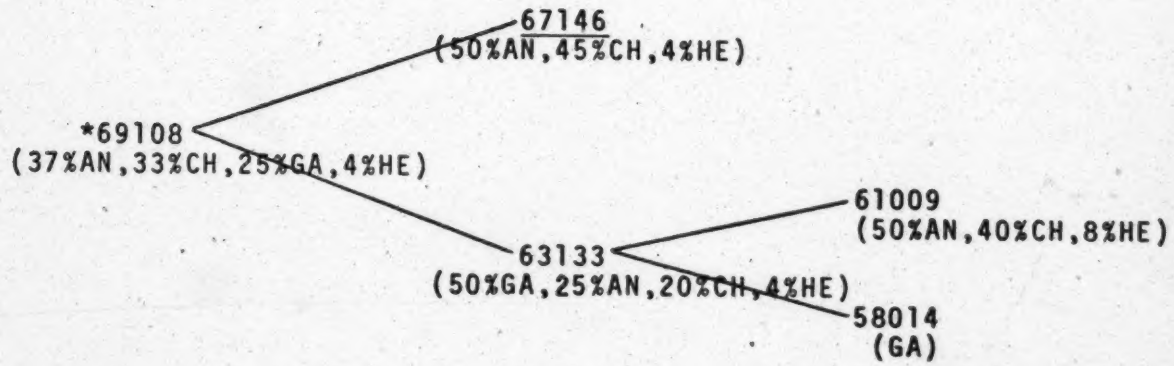


Chart D Cont'd.





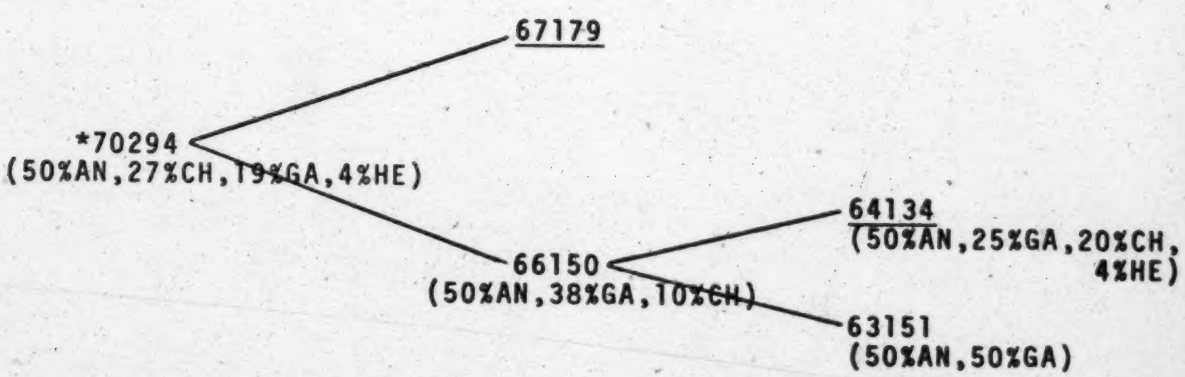
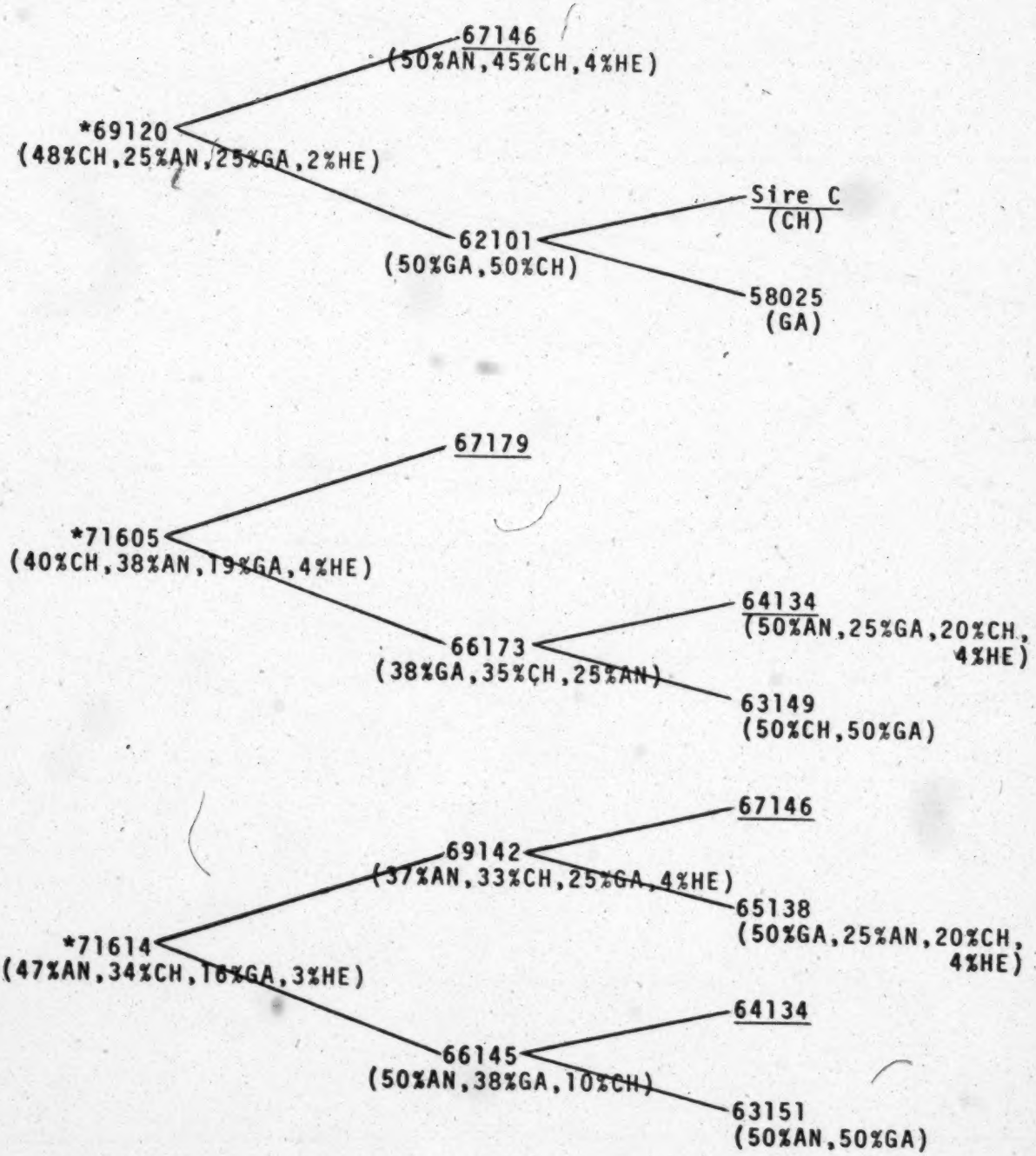


Chart D Cont'd.



All sires underlined have been referred to in Charts A,B&C.

to produce a crippled calf and the gene must be independently present in the parents. These pedigrees demonstrate the introduction of the defective gene into the population through cross-breeding to Charolais, and are compatible with a theory of homozygous recessive inheritance.

3.5 Differences between sexes

There appears to be no differences in the frequency of the defect between sexes as both males and females are affected. In this study, of the 26 crippled calves, 10 defective males and 14 defective females were observed. The sex of two crippled calves was not determined. No statistical analysis was carried out.

3.6 Differences between years

The defective calves in the herd started appearing in 1966 and there seem to be no association between the incidence of the disease and a particular year. Hence an environmental basis due to adverse conditions does not seem probable. Furthermore, all dams in the population were Charolais crosses from the same origin. Other breeding populations in the same herd had no defective calves.

3.7 Inbreeding effects

One other factor which favours a genetic cause is when inbreeding results in defective progeny. Sire A was plan mated on three occasions to his daughters in one breeding year and all three times the cross resulted in a defective calf.

3.8 Genetic analysis of arthrogryposis

3.8.1 Materials and methods

Two approaches were made to study the genetics of arthrogryposis. In the first, all calves from the 20 proven carrier dams born between 1961 and 1973 were used. The number of normal and defective calves, the number of matings between proven carrier males and females, and the total number of matings which included the proven carrier matings, suspected carrier matings and others were recorded during the experimental period. A proven carrier mating would be one where both sire and dam have been identified positively as carriers of the defective gene.

The second approach was to assess the frequency of defective calves born from a segregated herd of cripple carriers and suspects for the four calving seasons from 1970-1973 inclusive. In 1969-70 a herd consisting of both proven and suspects (usually sons and daughters of carriers) were drawn from the hybrid line and plan mated to carrier and suspected and carrier sires. This procedure was followed during the subsequent calving years and the data accumulated over a four year period are presented.

The sires and dams used in the study were weighted according to the probability of each individual transmitting the defective gene to its offspring. Accordingly, a homozygous carrier was assigned a probability rating of 1.0, a heterozygous carrier 0.5, a suspected carrier (offspring of a proven carrier) 0.25, a suspected carrier which had as its grand sire or grand

dam a proven carrier 0.125 and a suspected carrier having a suspected carrier as its grand sire or grand dam was rated 0.0625. During the experimental period of four calving seasons 131 calvings were recorded.

3.8.2 Results

Table 2 shows the number of defective and normal calves born in the herd by year and by sex.

Table 3 shows the kind or type of mating that took place during the experimental period in the first study. A total of 104 successful matings (matings which resulted in a calf being born) took place of which 50 were by proven carrier by carrier matings and 54 were by suspected and other sires. Of the 50 carrier by carrier matings 26 crippled calves were born. These results indicate that 52% of the known carrier by carrier matings produced defectives while 25% of the total number of matings resulted in defective offspring.

The details of calculation for the second study are shown in Appendix Table 1. The probability of each sire and dam transmitting the defective gene to its offspring together with the number identifying each sire and dam is shown by year. For the analysis the probabilities of each mating resulting in a defective calf were summed by sex and the mean probability calculated. The expected percentage of defectives from a cross of this type, assuming a recessive type of inheritance was then compared with the actual number of defective calves obtained in the population throughout the experimental period by a Chi-square

TABLE 2. Numbers of normal and crippled calves by sex and by year from the crippled herd

Year	Normal calves	Abnormal calves	Abnormal males	Abnormal females	Undetermined
1963	3	-	-	-	-
1964	4	-	-	-	-
1965	3	-	-	-	-
1966	3	1	-	1	-
1967	5	-	-	-	-
1968	12	-	-	-	-
1969	7	6	3	3	-
1970	13	4	1	2	1
1971	9	7	3	4	-
1972	12	2	1	1	-
1973	10	6	2	3	1
Totals	78	26	10	14	2

TABLE 3. Percent cripple calves born by two types of mating combinations from proven carrier dams

No. of proven carrier matings	Total No. matings	No. of crippled calves	% Cripples on proven carriers	% Cripples on all matings
50	104	26	52.0	25.0

analysis using Fisher's exact method for 2 x 2 tables.

3.8.3 Discussion

As indicated in Table 3, the deviation of the observed from the expected in proven carrier matings is high. A 52% value for defectives is observed while the expected value would be 25%, with complete penetrance of the gene in the recessives. Lauvergne (1972-73) indicated the penetrance of the defective gene in Charolais populations to be 0.14 among males and 0.1 among females.

There are some possible reasons why such a deviation may occur. Firstly, the sample size may be inadequate as on an average only two matings with proven carrier sires per proven carrier dam have been recorded. Thus the estimate of 52% defective may be biassed as the carrier dams have not been given enough opportunities to produce normal offspring as well. Lasley (1965) reported that assuming complete penetrance of a recessive gene, to test a male for heterozygosity on carrier dams at least 11 matings are required at $P < 0.05$ and 16 matings per sire at $P < 0.01$. Secondly there is a possibility that some of the carriers especially the sires are homozygous recessive for the character in question although they do not manifest the symptoms of arthrogryposis.

Since the estimate of 52% defectives is biassed it would be more accurate to take into account all mating combinations and see what proportion of these resulted in defective calves. On a total of 104 matings 26 crippled calves were born indicat-

ing that 25% of the offspring were defective. This figure is still probably biassed upward because of using only proven carrier dams in the study.

As most of the dams in which the defective gene has not been detected are either daughters of carriers or dams selected according to pedigree and are suspected of carrying the recessive gene, including them in an over all study would be more meaningful and hence the second study was designed and undertaken. As this analysis took into account a larger population of both suspected and proven males and females it should provide more information of the method of gene inheritance and the penetrance of the arthrogryposis gene in the population.

The results indicate the mean probability for sires in the population over 131 successful matings to be 0.3807 reflecting that the population consisted of sires that were proven as well as suspects in almost equal proportions. The mean probability for dams was 0.3115 reflecting a higher proportion of suspect dams than proven carriers in the population.

In a trait that is inherited as an autosomal recessive, assuming complete penetrance of the gene in the homozygote, a carrier by carrier mating would result in 25% of the individuals being born defective. Similarly, in the experimental situation, assuming a recessive form of inheritance 11.85% defectives could be expected if the males and females had probabilities of 0.3807 and 0.3115 respectively. However during the experimental period of four years 19 defective calves were obtained from 131

successful matings (Table 2) or 14.5% were defective. On a Chi-square analysis using the observed and expected values, no significance was found suggesting that the observed fits the expected or that the two samples were drawn from the same population.

The study suggests that arthrogryposis conforms to a recessively inherited type of abnormality and that the penetrance of the gene is high and near complete in the experimental population. It also confirms that the frequency of carriers is high in this herd.

3.8.4 Conclusion

Evidence from these analyses tend to agree with the work done by Lauvergne, (1969) indicating that arthrogryposis is genetic and caused by the action of an autosomal recessive gene. However the gene seems to show a high degree of penetrance in the present data unlike the situation reported by Lauvergne where penetrance was very low.

4. AN EVOLUTIONARY HYPOTHESIS FOR THE PERSISTENCE OF ARTHROGRYPOSIS IN CHAROLAIS CATTLE

4.1 Reasons why deleterious genes persist in populations

The recessive gene responsible for arthrogryposis seems to persist in Charolais populations at a high frequency in spite of its adverse effects. The disease has been recognized as being stationary and common in Charolais populations (Lauvergne, 1972-73). There are several reasons why a deleterious gene might persist in a population, especially at an above normal frequency. Recurrent mutation would tend to keep the gene present at a low equilibrium frequency through successive generations. Secondly, some form of assortative mating or frequency dependent selection could allow the arthrogryposis gene to persist in populations. Thirdly, it may persist due to a selective advantage that the heterozygotes possess with respect to some important fitness character. Lauvergne (1972-73) indicated that the arthrogryposis gene may have a selective advantage if hybrid vigour related to reproduction is involved.

The object of this investigation was to examine whether heterozygous dams do have a selective advantage with respect to characters associated with reproductive performance over a control stock of the same genetic background. If this be the case it would explain why an abnormal recessive gene persists in a population in spite of its adverse effects.

4.2 Experimental evidence

4.2.1 Materials and methods

Fertility and longevity were compared in the population of confirmed arthrogryposis carrier dams and a control stock of hybrid dams of a similar genetic background. The arthrogryposis carrier or cripple herd was derived from this hybrid herd used as the control.

As mentioned previously, 20 confirmed carrier dams have been identified which range in Charolais breeding from 10 to 75%. The data were collected from 1961 to 1971 on these 20 dams as well as the control population. All management practices in the two populations were similar, (Berg, 1973).

The control herd consisted of 401 dams which were in the same age groups as the dams in the cripple population. All dams that were in the herd during the whole or part of the experimental period were included. Hence, the dams that were culled for various reasons during the early, middle or late years as well as those still existing in the two populations were evaluated. The reason for including the culls and the dams still productive in the herd was to get an unbiassed estimate of the two characters under study. If only those dams that were productive up to 1971 were evaluated and the culls left out, this would have to be considered a sample in which selection had been practiced and true values of fertility and longevity would not have been reflected. There was however a certain amount of selection practiced in the hybrid herd during the

latter years in that a dam was allowed only two missed calving opportunities throughout its breeding life. Using this basis the dams were culled unless there was a valid reason for keeping a dam that missed two calving opportunities. In other words there was selection for better reproductive performance being practiced within the herd during the latter years.

For comparing longevity in the two populations, it was defined as the number of years a dam had successfully produced a calf allowing a maximum of one missed opportunity, and up to the time it missed its second calf. For example, if a dam missed its first and sixth calf its breeding life would be five years, up to the time it missed its second calf. The reason for following this procedure was to make a comparable assessment of longevity as the cripple herd had never more than one missed calving opportunity, while some cows in the control herd had up to three missed calves. In the estimation of fertility however, each dam's entire life history was considered irrespective of how many missed opportunities she had. The dams were bred as yearlings in the summer so that they calved during spring the following year. One breeding year was taken to be from July - August of one year to July - August of the following year. Records were kept on animals from the time they were past one year of age which corresponded to their first breeding exposure.

4.2.2 Measure of fertility

Fertility was estimated in the two populations by measuring the number of missed opportunities of each dam over the 11 breed-

ing years, over the number of dams eligible to be bred during each breeding year. The number eligible during each breeding year consisted of those dams that were old enough to be bred. For example, 401 dams in the control population were eligible to be bred or to produce their first calf, while only 334 dams were eligible to produce their second calf or bred for the second time. This means that 67 dams were too young to produce a second calf or to be bred a second time, as they would be the dams born in 1971. Hence each year one group of dams born in the latter years would be eliminated as the two herds consisted of dams born from 1961 to 1971.

A successful mating was a union where a calf was born irrespective of the condition of the calf and whether or not it survived.

4.2.3 Measures of longevity

Longevity was evaluated in the two populations by comparing the dams culled for all reasons (all culls), and the dams culled due to reproductive reasons, over the total number of dams in the two herds during the experimental period. The dams culled due to reproductive reasons included those that missed calving on two separate occasions while dams culled for all reasons included in addition those culled for age and disease. Those dams lost or unaccounted for were not considered in the evaluation of either fertility or longevity. A higher proportion culled would mean that there were less dams available for breeding, a short breeding life per dam and lower longevity.

4.2.4 Method of analysis

Probabilities were calculated using a Chi-square analysis applying Fisher's exact method for 2 x 2 tables. For fertility, a pooled estimate of the number of missed opportunities on the total number of eligible matings during the entire period was compared in the two populations. For longevity, a pooled estimate of the dams culled due to all causes and the dams culled due to reproductive causes on the number of dams in the two populations during the entire period was compared to establish significance.

4.2.5 Results

Table 4, shows the total number of dams eligible to be bred during the 11 breeding years, the number of missed opportunities and the percent misses in the control and cripple populations.

In the control herd, a total of 261 opportunities were missed over 11 breeding years on 2,013 possible matings, while 5 opportunities were missed on 116 possible matings in the cripple herd.

Table 5a, shows the number and percent dams culled within each breeding year on the total eligible during each breeding year. Tables 5b and 5c show a break down of the number of dams culled by each breeding year and by each dam year in the control and cripple herds respectively.

Tables 6a and 6b, show the number of dams within each dam year, the number and percent culled due to all causes, and the number and percent culled due to reproductive causes, in the

TABLE 4: The number of misses and the % misses on the total eligible by each breeding year in the control and cripple populations

	Control			Cripple		
Breeding year	Total eligible	Misses	%	Total eligible	Misses	%
1	401	58	14.46	20	-	-
2	334	82	24.56	18	2	11.11
3	280	37	13.21	17	1	5.89
4	236	21	8.90	14	2	14.29
5	211	20	9.48	13	-	-
6	164	11	6.71	12	-	-
7	130	14	10.77	6	-	-
8	104	7	6.73	5	-	-
9	75	7	9.33	4	-	-
10	54	3	5.56	4	-	-
11	24	1	4.17	3	-	-
Total	2013	261	12.97	116	5	4.31

TABLE 5a: The number and percentage of dams culled on the total eligible by breeding year in the 2 herds

	Control			Cripple		
Breeding year	Total eligible	# Culls	%	Total eligible	# Culls	%
1	401	45	11.22	20	-	-
2	334	55	16.44	18	-	-
3	280	44	15.71	17	1	5.89
4	236	8	3.39	14	-	-
5	211	17	8.06	13	-	-
6	164	13	7.93	12	-	-
7	130	13	10.00	6	-	-
8	104	9	8.65	5	-	-
9	75	5	6.67	4	-	-
10	54	4	7.41	4	2	50.0
11	24	1	4.71	3	-	-

TABLE 5b: The number of dams culled by breeding year and dam year in the control herd

	Dams culled/Breeding year											
Dam Year	1	2	3	4	5	6	7	8	9	10	11	Total
1961	1	2	4	1	0	6	3	2	0	4	1	24
1962	0	4	4	0	6	1	4	0	3	-		22
1963	1	2	1	0	0	1	2	5	2			14
1964	2	1	4	1	4	0	3	2				17
1965	4	8	1	1	2	4	1					21
1966	8	3	2	3	4	1						21
1967	4	6	13	2	1							26
1968	5	3	9	0								17
1969	5	11	6									22
1970	12	15										27
1971	3											3
Total	45	55	44	8	17	13	13	9	5	4	1	214

TABLE 5c: The number of the dams culled by breeding year and dam year in the cripple herd

	Dams culled/Breeding year											
Dam Year	1	2	3	4	5	6	7	8	9	10	11	Total
1961	-	-	-	-	-	-	-	-	-	2	-	2
1962	-	-	-	-	-	-	-	-	-	-		-
1963	-	-	-	-	-	-	-	-	-			-
1964	-	-	-	-	-	-	-	-				-
1965	-	-	-	-	-	-	-					-
1966	-	-	1	-	-	-						1
1967	-	-	-	-	-							-
1968	-	-	-	-								-
1969	-	-	-									-
1970	-	-										-
1971	-											-
Total	-	-	1	-	-	-	-	-	-	2	-	3

TABLE 6a: The number of dams in the control herd by each dam year, number and percent culled due to all reasons and the number and percent culled due to reproductive reasons on all culls

Dam Year	No. in Herd	Culled - All Causes No.	Culled - All Causes %	Culled - Reproductive No.	Culled - Reproductive %
1961	24	24	100.00	16	66.67
1962	30	22	73.33	17	77.27
1963	21	14	66.67	8	57.14
1964	29	17	58.62	16	94.12
1965	26	21	80.77	17	80.95
1966	34	21	61.76	17	80.95
1967	47	26	55.32	22	84.62
1968	25	17	68.00	10	58.82
1969	44	22	50.00	17	77.27
1970	54	27	50.00	21	77.78
1971	67	3	4.48	3	100.00
Total	401	214	53.37	164	76.64

TABLE 6b: The number of dams in the cripple herd by each dam year, number and percent culled due to all reasons and the number and percent culled due to reproductive reasons

Dam Year	No. in Herd	Culled - All Causes No.	%	Culled - Reproductive No.	%
1961	3	2	66.67	-	-
1962	1	-	-	-	-
1963	-	-	-	-	-
1964	1	-	-	-	-
1965	1	-	-	-	-
1966	6	1	16.67	-	-
1967	1	-	-	-	-
1968	1	-	-	-	-
1969	2	-	-	-	-
1970	1	-	-	-	-
1971	3	-	-	-	-
Total	20	3	15.00	-	-

control and cripple populations respectively.

There were 53.37% dams culled due to all causes in the control herd while 15.0% were culled in the cripple herd during the same period. None of the dams in the cripple herd were culled due to reproductive reasons while 76.64% of all those culled were due to these reasons in the control herd.

The probability that the number of missed opportunities based on the total number of possible matings in the two herds coming from the same population is 0.004. Hence it is concluded that the two herds differ significantly in fertility, the cripple herd having less missed opportunities than the control herd, ($P < 0.01$).

The probability of the number of dams culled due to all causes based on the number of dams in each herd during the trial being drawn from the same population is 0.001. This would indicate that, significantly more dams were culled in the control herd, ($P < 0.01$). Thus the dams in the cripple herd had longer breeding lives as they remained in the herd longer than those in the control herd. The analysis also indicated that significantly less dams were culled due to reproductive reasons in the cripple population when compared to the control population, ($P < 0.01$).

4.2.6 Discussion

From this study it is clear that arthrogryposis carrier dams show a more successful and longer breeding life when compared to a control of a similar genetic background. The carrier

dams therefore would more likely, produce a calf each year without many missed opportunities and be productive in herds for longer periods of time. For instance, none of the arthrogryposis carrier dams had more than one missed calf which demonstrates their better reproductive performance. During the experimental period as seen from Table 4a, 12.97% missed breeding opportunities were observed in the control herd while only 4.31% missed opportunities were recorded in the cripple carrier herd.

Longevity on both counts, dams culled due to all causes and dams culled due to reproductive reasons was significantly superior in the cripple herd. Furthermore, none of the dams in the cripple herd were culled due to any reproductive failure. It is also interesting to note that of the three dams culled in the cripple herd two were born in 1961 and hence would be 12 years old. These two dams were not bred during the last year due to age, but given the opportunity there was a very good chance they might have been fertile enough to produce yet another calf. To illustrate their continued productive life, 85% of the arthrogryposis carrier dams are still productive in the herd and one dam born in 1961 has produced 10 calves over 11 breeding years and is still in production. In contrast, in the control herd over 50% of the dams have been culled due to all reasons during the experimental period of which, 76.64% have been culled due to reproductive reasons.

One reason for the high and stationary frequency or the persistence of the gene in populations, as reported by Lauvergne,

(1972-73), is because of the selective advantage that the arthrogryposis carrier dams have with respect to characters associated with reproductive fitness. As seen from these data the carrier dams showed superiority in both fertility and longevity over their contemporaries, which provides evidence in favour of Lauvergne's hypothesis.

4.2.7 Conclusion

In conclusion the results of the analyses demonstrate the superiority of the arthrogryposis carrier dams with respect to characters associated with reproduction, namely fertility and longevity, when compared to a control population of the same origin and genetic background.

One primary reason why a deleterious gene might persist in a population is confirmed in these data by the fact that the heterozygous dams showed heterosis for reproductive traits and hence a selective advantage.

4.3 Penetrance and expressivity

Certain genotypes that carry a mutant gene in the dominant or recessive form fail to produce the expected phenotypic effect. This phenomenon is referred to as incomplete penetrance. Penetrance of a gene is the frequency of the actual expression of a trait as compared with the frequency at which it is expected to be expressed, Lasley (1965). Penetrance is therefore the ability of a gene to express itself in the individuals that possess it usually in the homozygotes.

Expressivity is the degree of severity or expression of the character in the given individual of the particular genotype. As a consequence expressivity can be variable and penetrance can be complete or incomplete. Penetrance thus refers to the presence or absence of gene expression regardless of the degree, while expressivity applies to the variability of the expression of the condition.

4.3.1 Penetrance and expressivity of the arthrogryposis gene

The penetrance of the defective gene is reported to be incomplete, low and around 0.14 in males and 0.1 in females in French Charolais herds, Lauvergne, (1972-73). However, evidence from the Kinsella population indicates the penetrance of the gene to be near complete. The defect seems to be more freely expressed when the resulting progeny constitute a mixture of breeds along with the Charolais. In other words, the defect shows up better when the resulting progeny are Charolais crosses. In our experimental population none of the defective progeny were pure and all crippled calves had Charolais breeding ranging from 25% to 75%.

Though this thesis does not report in detail the degrees of severity of arthrogryposis, the expressivity too is very variable. In a penetrant individual the gene expresses itself by crippling one or both pairs of limbs, by the presence or absence of a cleft palate and by showing these traits as moderate to severe abnormalities. Furthermore, even among the homozygous recessive bulls which are originally classed as free of

the trait, it will be shown that there is a slight expression of the defect which begins to show up with age. This view could further be justified by observing the results from the genetic analysis where the expected number of defective calves have been observed, as if the defective gene were completely penetrant. This high degree of penetrance of the arthrogryposis gene observed among Charolais crosses has not been reported elsewhere in literature.

4.3.2 Evidence for the existence of homozygous recessive sires

In the present data one of the Reference Sires was probably homozygous recessive. Sire A which was referred to earlier was plan mated on three occasions to his own daughters within one year and all three times a crippled calf resulted. If sire A was heterozygous half its daughters would be carriers but if it was homozygous all daughters would be carriers. If sire A was mated back to its daughters half its progeny would be crippled if it was homozygous recessive. Even though numbers are insufficient there is room to suspect that sire A was a homozygous carrier.

A more positive example of homozygosity in a sire was encountered in the herd of a cattleman in the district. In the spring of 1970 in this herd 7 cases of arthrogryposis associated with an incompletely developed palate occurred. The history of the herd was traced back to find out through which animal or animals the defective gene was introduced. In 1968 a purebred Charolais sire P was purchased. This bull was bred to a number

of non Charolais dams mainly Shorthorns, the resulting progeny being half Charolais crosses. In 1971 full French Charolais sire Q was purchased and used on some yearling and two year old heifers, which included among them the 15 half Charolais cross daughters of sire P. In 1972 a total of 32 calves were born through sire Q, 15 of which came from the half Charolais daughters of sire P. Of these 15 calves, 8 were normal while 7 were crippled. This approximates closely to a 50:50 ratio of normal to crippled calves.

If the condition is recessive both parents must be carriers to drop a crippled calf. Hence, all the half Charolais daughters of sire P would be carriers only if one parent were homozygous recessive. It would appear likely that sire P was the double recessive parent as most of the dams used in the cross were Shorthorns. A 50:50 ratio of normal:defective calves is expected in a test cross where the heterozygote is mated to the recessive parent. When the daughters of sire P were crossed to sire Q, 7 of the 15 calves born were defective. The observed ratio indicates that sire Q was probably a homozygous recessive carrier of the defective condition. If sire Q were heterozygous only 25% would be crippled if there was complete penetrance of the gene in the homozygote offspring. An interesting observation is that sire Q had very poor front legs and was barely able to stand up and walk around. Furthermore, all progeny from the cross between the daughters of sire P and sire Q had very weak fore limbs up to two weeks after birth. A third case could be

cited referring to a case encountered by a cattleman in Saskatchewan. Thirty heifers were purchased by him, the heifers being from three pure Charolais sires referenced X, Y and Z. The heifers were either 1/2 Charolais Hereford crosses or 3/4 Charolais Hereford crosses. Of the 30 heifers purchased 18 were through sire X, 10 through sire Y and 1 through sire Z. The pedigree information on one heifer was not available and therefore not recorded.

In 1969 the 29 heifers were exposed to breeding and they produced 11 defective calves with confirmed symptoms of arthrogryposis and a cleft palate. Ten defective calves were from the daughters of sire X and 1 defective calf from the daughter of sire Z. No defective calves were obtained through the daughters of sire Y. Though the breeding combinations of the 29 heifers is not available to identify another carrier sire, the case indicates that sire X had passed down the recessive gene to at least 10 of his daughters and possibly to all his daughters if it were a homozygous recessive carrier of arthrogryposis. It is evident that the defective gene was introduced into the heifers through the pure Charolais sire X as almost all his mates have been Hereford dams. From the examples cited it would indeed be very probable that homozygous recessive sires exist, which appear normal in their phenotype.

The four examples cited, sires A, P, Q and X which show almost zero penetrance of the gene have all been pure Charolais bulls and all progeny showing the defect and consequently, apparent full penetrance of the gene have been Charolais crosses.

4.3.3 Modifier gene action

If the inheritance of arthrogryposis is controlled by an autosomal recessive gene the variable penetrance and expressivity is probably influenced by modifier genes. Modifiers present in the pure Charolais breed seem to control the penetrance of the homozygous genotype to a low frequency. In the presence of part of a gene complement from other breeds, penetrance becomes almost complete. There is reason also to suspect that expressivity is also less extreme or more controlled with a Charolais genetic millieu.

4.3.4 Conclusions

(1) It can be concluded that arthrogryposis in the population studied is conditioned by an autosomal recessive gene.

(2) Penetrance in pure Charolais populations is quite low.

(3) Expressivity of the homozygous condition is variable.

(4) Among Charolais crosses the defect is expressed more freely and the penetrance is near complete as the recessive gene complements do not have the right genome (combination of modifier genes).

(5) Two types of carriers distribute the gene in populations, the heterozygous or true carriers and the homozygous recessive carriers.

4.4 An evolutionary explanation for the persistence of the arthrogryposis gene in populations

A deleterious recessive gene may persist in a population due to recurrent mutations, assortative or selective mating,

frequency dependent selection or due to a selective advantage among the heterozygotes with respect to a primary fitness character. This concept can also be viewed through an evolutionary approach. Selection under natural conditions will favour characters that tend to increase the mean fitness of a population in order to ensure the continuity of the species.

4.4.1 Selective heterozygote advantage

Two mechanisms that help keep the defective arthrogryposis gene in herds has been recognized in the Charolais breed. The first mechanism the breed has evolved is to have arthrogryposis carrier dams showing a selective advantage in characters associated with reproductive fitness. As indicated previously in this thesis the carrier dams do show better fertility and longevity when compared to a control population of the same origin and genetic background. Hence, by evolving such a mechanism from within the population, the dams have a better chance of ensuring the continuity of the breed, line or family even though some calves have an inherent survival problem.

Through artificial selection if man were to mate best to best for the betterment of economic characters the arthrogryposis carriers would be selected as breeding stock and consequently a form of selective or assortative mating would contribute to the persistence of the defective gene in populations.

4.4.2 Suppression of the defect in recessive homozygotes

This mechanism is extreme and is the complete or near complete suppression of the defect among homozygous recessive ani-

mals. Due to the selection and accumulation of favourable gene modifiers, a few bulls in which the defect has been suppressed have been identified. However, it is only the pure Charolais animals that have evolved this mechanism by which they over come an inherent genetic defect, as when the homozygotes are crossbred the gene penetrance is almost complete. It is therefore not difficult to visualize the trend in evolution, and even at the present time some sires which are suspected of being homozygous recessive carriers tend to go lame with age, which indicates that the gene shows some effects in these animals.

It would seem very probable that the crippled gene has been in the Charolais for a long time, as they have evolved mechanisms that ride over the inherent defect, allows the gene to persist in the populations and ensures the continuity of the breed, line or family.

4.4.3 Conclusions

In evolutionary terms the Charolais breed has overcome the inherent genetic defect by two methods, and thereby the gene persists in the population. By the selective advantage that the carrier dams possess in reproductive fitness characters, continuity and increased frequency is assured. Arthrogryposis is not new to the Charolais breed and the animals have developed mechanisms by which the homozygous expression of the gene is almost completely suppressed by the accumulation of favourable modifier genes. Hence, the frequency of the carriers are

high while the frequency of the defective calves is low. This mechanism whereby a homozygous recessive does not express a genotypic abnormality in the phonotype is an extreme case of modification and will help to keep the defective gene in a population at high frequencies. The example therefore is a case of visual operative evolution resulting in improved adaptation of the breed.

Crossbreeding which results in homozygosity for the defective gene, results in increased penetrance because of the absence of some of the useful modifiers normally present in the Charolais breed.

5. THE PRACTICAL SIGNIFICANCE OF ARTHROGRYPOSIS

In its practical application there are two possible courses of action that one could take. Firstly, the gene could be eliminated from the herd or reduced to a low frequency and secondly, the gene could be controlled to utilize its advantageous effects.

5.1 Eliminate the gene or reduce the frequency

Complete elimination of the defective gene from Charolais populations is not practical as it would not only involve a long period of time but also be uneconomical to do so. However the frequency of the defective gene could be effectively controlled by regulated selection and breeding. Since the inheritance of the abnormality is of an autosomal recessive type, both parents must contribute equally. The first line of defense would be to use proven clean bulls for breeding in Charolais populations. By observing their pedigrees and eliminating all suspects from a breeding program the frequency of the gene could be kept low in a population. Since the defect is introduced through the Charolais, using non Charolais sires for breeding will subsequently reduce the frequency of the defective gene in herds.

5.2 Control the gene and utilize its good effects

It is my view that this would be the obvious choice as the former is almost impossible especially for Charolais breeders.

Though the penetrance of the gene appears to be high in Charolais crossbred herds, this should not discourage cattlemen

from the idea of crossbreeding for the improvement of economic characters. An obvious method to control the defective gene in a herd is to use clean bulls on dams in a breeding operation. With the increased emphasis given to Artificial Insemination in Canada it is possible to provide semen from bulls free of the defect which could be used on dams.

If Charolais bulls are used for breeding from within a farmer's herd on non Charolais females one must be careful when breeding from the F(1) as recombination occurs only in the F(2). Another practical method by which the gene could be controlled is by not using the same sire to breed during two successive generations. This will control the distribution of the recessive gene if the sire himself was an unidentified carrier.

The most assured means of controlling the defect is by identifying carriers and not allowing them to interbreed. As arthrogryposis is spread in herds by two types of carriers identification of the two types would be difficult. In order to recognize heterozygous 'true carriers' the classical approach of pedigree observation and progeny testing if possible could be advocated. However correct identification of carriers is difficult by these methods and in many instances they could complete their breeding life and still go undetected. This could particularly be true of females as they have lesser opportunities of expressing a recessive condition which is masked.

There appears to be no known way by which carriers could be identified but the homozygous recessive carriers may be recognized as they tend to go lame with age.

The better fertility and longevity that the arthrogryposis carriers have could be one economic character that a cattleman could utilize. It will be useful in a breeding herd as the females will be consistent and persistent in calving. However one problem which is basic would be to identify carriers. Since a carrier can be correctly identified if it produces a defective calf and since planned matings using clean bulls is being advocated positive identification will be very difficult.

If on the other hand a homozygous sire could be recognized early in life all his daughters will be carriers and by this means a carrier herd could be established. Animal breeders are aware that improvement in economic traits must come through breeding and selection in populations that show wide variability. Once carrier dams are obtained by using other bull breeds on these dams one could ensure that no defective progeny will be obtained. A dam that is fertile and productive over a long period of time could fit into any breeding population whether it be a single breed cross, a three way or a rotational cross.

Finally, inspite of its deleterious effects the gene has something to offer from a practical stand point if the carriers can be identified by a method involving less time. Though the economics have not been worked out, would it be better to have a dam which is productive over long periods and fertile that produces a defective calf out of every eight or ten, rather than to have a dam which is productive for a few years and has many missed calving opportunities?

6. RESEARCH IN ARTHROGRYPOSIS FOR THE FUTURE

It would be a very interesting study to see if there is any association between the expressivity of arthrogryposis and the degree of Charolais breeding among crossbreds. In my opinion as the degree of Charolais breeding decreases, the defect should be more fully expressed up to a maximum within a range, as the modifier genes controlling the expression of the defect should be in proportion to the amount of Charolais breeding.

In order to utilize the advantages associated with arthrogryposis or to avoid its disadvantages, all carriers should be identified. Since progeny testing males, unless done on a commercial scale, is not practical, the discovery of a more basic biochemical or physiological method to identify carriers would be useful.

In the late 1950's dwarfism in beef cattle was an important character and much work was done to recognize carriers by nongenetic methods. Emmerson and Hazel (1956) used anatomical methods by comparing the thoraco-lumbar spine in dwarf, dwarf carriers and normal calves as a method of identification of carriers. Biochemical methods involving differential blood sugar levels among carriers and non-carriers was reported by Blood and Henderson (1968).

However, in the case of arthrogryposis a basic enzyme system should be assessed to differentiate between carriers and noncarriers. If by these methods the carriers could be identified, the abnormality could be effectively controlled in populations.

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APPENDIX TABLE 1. THE PROBABILITIES OF EACH SIRE AND DAM PASSING DOWN THE RECESSIVE ARTHROGRYPOSIS GENE TO ITS OFFSPRING

Year 1969-70

Sire	P	Dam	P
67179	0.5	3-1	0.25
68360	0.0625	7-1	0.5
67179	0.5	11-1	0.25
67179	0.5	12-1	0.5
67179	0.5	106-5	0.25
67179	0.5	122-4	0.5
67179	0.5	107-6	0.5
68137	0.25	133-6	0.25
67179	0.5	135-6	0.5
67179	0.5	145-6	0.5
67179	0.5	150-6	0.25
67179	0.5	159-6	0.25
68137	0.25	173-6	0.25
66137	0.25	105-7	0.25
66128	0.125	107-7	0.125
67283	0.125	144-8	0.25
68134	0.0625	150-8	0.125
67283	0.125	167-8	0.25
68137	0.25	168-8	0.25
67179	0.5	250-5	0.25
67179	0.5	271-6	0.25
Sire (A)	1.0	244-6	0.125

Year 1970-71

Sire	P	Dam	P
69115	0.25	2-1	0.25
69115	0.25	3-1	0.25
67179	0.5	4-1	0.25
69142	0.25	7-1	0.5
67179	0.5	8-1	0.25
69142	0.25	11-1	0.5
69142	0.25	12-1	0.5
67179	0.5	101-2	0.25
67179	0.5	102-2	0.25
69115	0.25	106-3	0.25
69142	0.25	122-4	0.5
69115	0.25	101-5	0.25
67179	0.5	134-5	0.25
67179	0.5	250-5	0.25
69142	0.25	107-6	0.5
69115	0.25	133-6	0.25
69142	0.25	135-6	0.5
69142	0.25	145-6	0.5
67179	0.5	150-6	0.25
69115	0.25	155-6	0.25
69115	0.25	159-6	0.25
67179	0.5	173-6	0.25
69115	0.25	271-6	0.5

Year 1970-71 Cont'd.

Sire	P	Dam	P
67179	0.5	105-7	0.25
69115	0.25	118-7	0.25
69171	0.03	114-7	0.25
67179	0.5	105-8	0.0625
69115	0.25	106-8	0.0625
68140	0.03	107-8	0.0625
68140	0.03	144-8	0.25
68140	0.03	167-8	0.25
69115	0.25	168-8	0.25
69142	0.25	102-9	0.25
69115	0.25	105-9	0.25
69115	0.25	108-9	0.25
69142	0.25	113-9	0.25
69115	0.25	120-9	0.25
69142	0.25	123-9	0.25
69142	0.25	124-9	0.25
67179	0.5	165-9	0.25
69115	0.25	174-9	0.25
69142	0.25	185-9	0.25
69142	0.25	191-9	0.25

Year 1971-72

Sire	P	Dam	P
69115	0.5	2-1	0.25
69171	0.5	4-1	0.25
70153	0.25	7-1	0.5
69115	0.5	8-1	0.25
70175	0.125	11-1	0.5
69171	0.5	12-1	0.5
69171	0.5	101-2	0.5
70175	0.125	102-2	0.25
70153	0.25	106-3	0.25
70175	0.125	122-4	0.5
70153	0.25	101-5	0.5
70175	0.125	107-6	0.5
70153	0.25	135-6	0.5
70175	0.125	145-6	0.5
70153	0.25	150-6	0.5
69115	0.5	155-6	0.25
69115	0.5	159-6	0.25
69115	0.5	105-7	0.25
69171	0.5	105-8	0.0625
69171	0.5	106-8	0.0625
69142	0.25	144-8	0.25
69142	0.25	167-8	0.25
70153	0.25	168-8	0.5
69171	0.5	102-9	0.25

Year 1971-72 Cont'd.

Sire	P	Dam	P
70175	0.125	105-9	0.5
69171	0.5	120-9	0.25
69115	0.5	142-4	0.125
69171	0.5	142-6	0.125
69115	0.5	162-7	0.125
69115	0.5	286-0	0.25
69115	0.5	294-0	0.25

Year 1972-73

Sire	P	Dam	P
69115	0.5	12-1	0.5
"	0.5	101-2	0.5
"	0.5	102-2	0.25
"	0.5	106-3	0.25
"	0.5	122-4	0.5
"	0.5	101-5	0.5
"	0.5	107-6	0.5
"	0.5	135-6	0.5
"	0.5	142-6	0.125
"	0.5	145-6	0.5
"	0.5	150-6	0.5
"	0.5	155-6	0.25
"	0.5	159-6	0.25
"	0.5	105-7	0.25
"	0.5	114-7	0.5
"	0.5	162-7	0.125
"	0.5	106-8	0.5
"	0.5	168-8	0.5
"	0.5	105-9	0.5
"	0.5	108-9	0.5
"	0.5	120-9	0.25
"	0.5	286-6	0.25
"	0.5	294-0	0.5

1972-73 Cont'd.

Sire	P	Dam	P
69115	0.5	601-1	0.25
"	0.5	605-1	0.25
"	0.5	606-1	0.25
"	0.5	607-1	0.25
"	0.5	608-1	0.25
"	0.5	611-1	0.25
"	0.5	613-1	0.25
"	0.5	614-1	0.25
"	0.5	615-1	0.25
"	0.5	620-1	0.25
"	0.5	622-1	0.25
"	0.5	625-1	0.25